



# An unusual cause of diarrhea in a child with nephrotic syndrome: Questions

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Received: 29 April 2023 / Revised: 29 April 2023 / Accepted: 4 May 2023 / Published online: 24 May 2023  
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**Keywords** Child · Diarrhea · Nephrotic syndrome

## Case presentation

A ten-year-old patient with steroid-dependent and frequently relapsing nephrotic syndrome (NS) came to clinical attention with diarrhea. His medical history revealed that he was first diagnosed with NS at the age of two years and remission was achieved within a month of oral steroid therapy. He had experienced relapses at the second and fifth months of follow-up while on steroid weaning and a kidney biopsy was performed which showed minimal-change disease. Cyclosporine was introduced at the seventh month of follow-up and remission was achieved within 5 months. After one year, cyclosporine was switched to tacrolimus due to hypertrichosis; and steroid treatment was discontinued. Nevertheless, the patient experienced an NS relapse 3 months later, and prednisolone was restarted. On tacrolimus and prednisolone therapy, the patient experienced five relapses in a year, all of which responded to steroids. Considering the frequently relapsing nature of the disease, another kidney biopsy was performed which was unremarkable other than mild cellular expansion in the mesangium and glomeruli. Remission was achieved within a month with oral steroid at the last relapse,

and four doses of rituximab (RTX) were given at 375 mg/m<sup>2</sup> per week. Two more doses were given in the following year and remission was sustained; prednisolone treatment was tapered and discontinued.

Twenty months after the first and five months after the last RTX dose, the patient developed abdominal pain, foul-smelling diarrhea with mucus. His laboratory investigations showed an increase in acute phase reactants; metronidazole treatment was administered with a possible diagnosis of infectious enteritis. An extensive work-up was performed which revealed no obvious infectious cause. Laboratory investigations at the onset of diarrhea are summarized in Table 1.

The patient's diarrhea persisted; and turned into tenesmus and bloody diarrhea within two months. An increment in acute phase reactants was observed and fecal calprotectin level was significantly elevated. Total colonoscopy and endoscopy were performed which showed hyperemia, fragility, edema, decreased vascularity of the entire colonic mucosa with multiple ulcers. Colonic biopsy specimens showed mixed inflammatory cellular infiltration, edema, congestion, and crypt abscesses (Fig. 1).

The answers to these questions can be found at <https://doi.org/10.1007/s00467-023-06021-w>.

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## Questions

1. What are the possible causes of diarrhea in this patient?
2. What is your diagnosis and what could be the underlying mechanism?
3. How would you manage this patient?

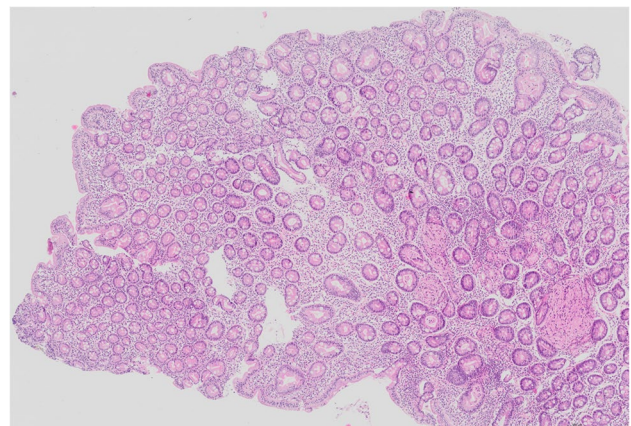
**Table 1** Laboratory findings

	Reference range	
Complete blood count		
Hemoglobin, g/dl	14.1	13.6–17.2
Red blood cells, 10 <sup>6</sup> /μL	5.08	4.38–5.77
MCV, fL	80.3	80.7–95.5
MCHC, g/dl	34.5	32.7–35.6
White blood cells, 10 <sup>3</sup> /μL	15.5	4.3–10.3
Platelet, 10 <sup>3</sup> /μL	372	156–373
Neutrophil, 10 <sup>3</sup> /μL	12.0	2.1–6.1
Lymphocyte, 10 <sup>3</sup> /μL	1.8	1.3–3.5
Monocyte, 10 <sup>3</sup> /μL	1.2	0.3–0.9
Eosinophil, 10 <sup>3</sup> /μL	0.4	0–0.2
Biochemistry		
Sodium, mEq/L	137	136–146
Potassium, mEq/L	3.70	3.4–4.7
Creatinine, mg/dl	0.49	0.26–0.77
Blood urea nitrogen, mg/dl	14.50	5–18
Uric acid, mg/dl	5.60	3.5–7.2
ALT, U/L	19	<39
AST, U/L	38	<51
GGT, U/L	19	42–362
Total bilirubin, mg/dl	0.45	0.3–1.2
Total protein, g/dl	7.65	6–8
Albumin, g/dl	4.98	3.5–5.2
Urinalysis		
pH	5.5	
Density	1026	
Protein	Negative	
Leukocyte	1	
Erythrocyte	1	
Other laboratory tests		
Glucose	Negative	
PCR, mg/mg creatinine	0.18	<0.20
ACR, mg/g creatinine	8.98	<30
CD19, %	0	
CD20, %	0	
C-reactive protein, mg/dl	7.07	0–0.8
ESR, mm/hour	28	0–20
Anti HAV IgM	Negative	
Anti-HAV Total	Negative	
HBs Ag	Negative	
Anti HBs Ab, mIU/ml	33.64	
Anti HBc IgM	Negative	
Anti HBc Total	Negative	
Anti HCV	Negative	
Anti-HIV	Negative	
CMV IgM, TU/ml	Negative	
Tissue transglutaminase IgA, RU/mL	Negative	
Stool examinations		
Fecal culture	Negative	
Reducing substance and pH	Negative	

**Table 1** (continued)

	Reference range	
Steatocrit	Negative	
Giardia lamblia	Negative	
Cryptosporidium	Negative	
Entamoeba histolytica	Negative	
Clostridium difficile Ag	Negative	
Calprotectin, μg/g	> 2100	0–50

ACR albumin-to-creatinine ratio; ALT alanine aminotransaminase; AST aspartate aminotransferase; BUN blood urea nitrogen; ESR erythrocyte sedimentation rate; GGT gamma glutamyl transferase; MCHC mean corpuscular hemoglobin concentration; MCV mean corpuscular volume; PCR protein-to-creatinine ratio



**Fig. 1** Colonic biopsy specimens showing active colitis features characterized with mixed inflammatory cellular infiltration, edema, congestion, and crypt abscesses (H&E staining)

**Data availability** All data have been presented in the manuscript.

**Code availability** Not applicable.

## Declarations

**Ethics approval** Not applicable.

**Consent for publication** An informed consent was obtained from the parents.

**Conflicts of interest** The authors have no relevant financial or non-financial interests to disclose.

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